

AMENDMENTS TO THE SPECIFICATION

On page 5, lines 13-15, please replace the original paragraph with the following amended paragraph:

~~Figure 2~~ Figures 2A-2D show the conjugate obtained was able to enter the eukaryotic cells in culture, wherein the mouse antiGLI IgG-Transportan TP10 conjugate is visualized (FIG. 2A), the mouse FITC-conjugated anti-IgG is visualized (FIG. 2B), the mouse anti-GLI1 (IgG)-Transportan TP10 conjugate is visualized (FIG. 2C), and the mouse FITC-conjugated anti-IgG is visualized (FIG. 2D).

On page 5, lines 17-20, please replace the original paragraph with the following amended paragraph:

FIG. 3A shows the production and purification of the cell penetrating recombinant GST-GL13(150-250)-9Arg fusion protein. The figure shows the image of Coomassie brilliant blue-stained SDS-polyacryl-amide gel. Lane 1: molecular weight marker. Lane 2: uninduced E. coli cell lysate; Lanes 3 and 4: cell lysate, where the expression of the construct has been induced by IPTG. Lanes 5-8: protein fractions 1-4 eluted from glutathione-agarose.

On page 5, lines 23-26, please replace the original paragraph with the following amended paragraph:

FIG. 3B shows the internalization of the recombinant fusion protein into human 293 cells. The cells were incubated with recombinant GST-GL13(150-250)-9Arg fusion proteins and fluorescent anti-GST antibodies (upper image) detected their internalization into the cells. The image below depicts the phase-contrast image of the same field.

On page 8, lines 9-18, please replace the original paragraph with the following amended paragraph:

Example 6. Developing a technology for obtaining recombinant cell penetrating proteins

For obtaining a recombinant cell penetrating protein we created expression vector encoding for GST-GL13(150-250) fusion protein. We used PCR based approach to add the sequences

encoding for cell penetrating peptides Transportan TP10 and 9Arg (9Arginine) (SEQ ID NO: 9) into previously mentioned vector. These expression constructs were sequenced. Expression of these constructs showed that despite repeated efforts, it was not possible to express a recombinant fusion protein that encoded GST-GLI3(150-250)-Transportan TP10 sequence described above in *E. Coli* system. We succeeded, though, in expressing and purifying a recombinant protein that encoded the recombinant GST-GLI3(150-250)-9Arg (SEQ ID NO: 9) cell penetrating peptide (figure 3A).

On page 8, lines 23-30, please replace the original paragraph with the following amended paragraph:

Example 7. Obtaining and characterisation of anti GLI recombinant proteins entering into the cell

The recombinant antibodies were obtained by inserting the sequence encoding for the 9Arg peptide (SEQ ID NO: 9) or Transportan or Transportan TP10 into the gene encoding the clones of antibodies described above. The obtained recombinant antibodies were purified using affinity chromatography and antibody titre was determined. We demonstrated that these antibodies were binding specifically to the GLI1 protein. These recombinant antibodies also entered into the eukaryotic cells in culture.

On page 9, beginning at line 15, please replace the original paragraph with the following amended paragraph:

PCR products of the appropriate size (320-350 bp) were purified and sequenced. Oligonucleotide primer encoding for Transportan or Transportan TP10 and linker (Gly4Ser)₃ (SEQ ID NO: 10) was used to construct a VL-TP-Linker-VH sequence by three-step overlap extension PCR. The process was repeated for scFvFc construction with relevant VLCL and VHCH1 PCR products. The final PCR products corresponding scFv and scFvFc (both with CPP and linker encoding) sequence were cloned into eukaryotic expression vector (pcDNA3, pCEP) and sequenced. Eucaryotic cells (Cos-7) were be transfected with scFv or scFvFc constructs and according to the

manufacturer's instructions for generation of stable cell lines. Recombinant proteins were purified from supernatant using Ni⁺ columns.